CYP2C9 gene

cytochrome P450 family 2 subfamily C member 9

Normal Function

The *CYP2C9* gene provides instructions for making an enzyme that is found in a cell structure called the endoplasmic reticulum, which is involved in protein processing and transport. The CYP2C9 enzyme breaks down (metabolizes) compounds including steroid hormones and fatty acids. The CYP2C9 enzyme also plays a major role in breaking down the drug warfarin, which thins the blood and prevents blood clots from forming. This enzyme also assists in metabolizing other drugs such as ibuprofen, which reduces inflammation.

Health Conditions Related to Genetic Changes

warfarin sensitivity

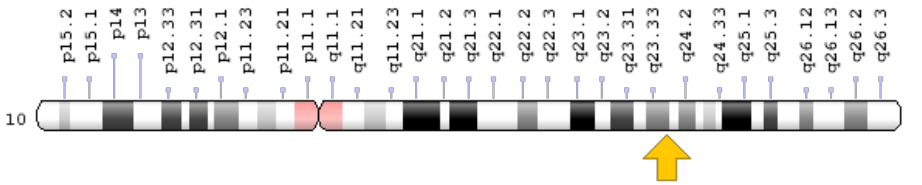
Certain common *CYP2C9* gene variations (polymorphisms) that decrease the activity of the CYP2C9 enzyme can result in a condition called warfarin sensitivity. The altered enzyme slows the breakdown (metabolism) of warfarin, allowing the drug to remain active in the body for a longer period of time. People with warfarin sensitivity take longer than usual to metabolize warfarin and may require lower doses of the drug than are usually prescribed.

The two most common *CYP2C9* gene polymorphisms change single protein building blocks (amino acids) in the CYP2C9 enzyme. The first one, known as *CYP2C9*2*, replaces the amino acid arginine with the amino acid cysteine at position 144, written as Arg144Cys or R144C. The *CYP2C9*2* polymorphism leads to a decrease in warfarin metabolism to such a degree that prescription doses are typically reduced by one-third in people with this variation. The second polymorphism, known as *CYP2C9*3*, replaces the amino acid isoleucine with the amino acid leucine at position 359, written as Ile359Leu or I359L. In people with the *CYP2C9*3* polymorphism, prescription doses are typically reduced by one-fifth. In rare cases in which individuals have both *CYP2C9*2* and *CYP2C9*3* polymorphisms, the enzyme activity is severely decreased and metabolism of warfarin is very slow. If people with warfarin sensitivity take the average dose (or more) of warfarin, they are at risk of an overdose, which can cause abnormal bleeding in the brain, gastrointestinal tract, or other tissues, and may lead to serious health problems or death.

Chromosomal Location

Cytogenetic Location: 10q23.33, which is the long (q) arm of chromosome 10 at position 23.33

Molecular Location: base pairs 94,905,867 to 94,989,395 on chromosome 10 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- CYPIIC9
- cytochrome P-450MP
- cytochrome P450 2C9
- cytochrome P450 MP-4
- cytochrome P450 MP-8
- cytochrome P450 PB-1
- cytochrome P450, family 2, subfamily C, polypeptide 9
- cytochrome P450, family 2, subfamily C, polypeptide 9 gene
- P450 MP-4
- S-mephenytoin 4-hydroxylase
- S-mephenytoin 4-hydroxylase, human
- warfarin-7-hydroxylase, human

Additional Information & Resources

Educational Resources

- Biochemistry (fifth edition, 2002): Blood-Clotting Cascade https://www.ncbi.nlm.nih.gov/books/NBK22589/figure/A1401/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28CYP2C9%5BTI%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

OMIM

- CYTOCHROME P450, SUBFAMILY IIC, POLYPEPTIDE 9
  http://omim.org/entry/601130

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_CYP2C9.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=CYP2C9%5Bgene%5D
- HGNC Gene Family: Cytochrome P450 family 2
  http://www.genenames.org/cgi-bin/genefamilies/set/1001
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=2623
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/1559
- The Human Cytochrome P450 (CYP) Allele Nomenclature Database: CYP2C9 Allele Nomenclature
  http://www.cypalleles.ki.se/cyp2c9.htm
- UniProt
  http://www.uniprot.org/uniprot/P11712

Sources for This Summary

- OMIM: CYTOCHROME P450, SUBFAMILY IIC, POLYPEPTIDE 9
  http://omim.org/entry/601130
- Ferder NS, Eby CS, Deych E, Harris JK, Ridker PM, Milligan PE, Goldhaber SZ, King CR, Giri T, McLeod HL, Glynn RJ, Gage BF. Ability of VKORC1 and CYP2C9 to predict therapeutic warfarin dose during the initial weeks of therapy. J Thromb Haemost. 2010 Jan;8(1):95-100. doi: 10.1111/j.1538-7836.2009.03677.x. Epub 2009 Oct 30.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19874474
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3718044/

- Flockhart DA, O'Kane D, Williams MS, Watson MS, Flockhart DA, Gage B, Gandolfi R, King R, Lyon E, Nussbaum R, O'Kane D, Schulman K, Veenstra D, Williams MS, Watson MS; ACMG Working Group on Pharmacogenetic Testing of CYP2C9, VKORC1 Alleles for Warfarin Use. Pharmacogenetic testing of CYP2C9 and VKORC1 alleles for warfarin. Genet Med. 2008 Feb;10(2): 139-50. doi: 10.1097/GIM.0b013e318163c35f.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18281922
- Moyer TP, O'Kane DJ, Baudhuin LM, Wiley CL, Fortini A, Fisher PK, Dupras DM, Chaudhry R, Thapa P, Zinsmeister AR, Heit JA. Warfarin sensitivity genotyping: a review of the literature and summary of patient experience. Mayo Clin Proc. 2009 Dec;84(12):1079-94. doi: 10.4065/mcp.2009.0278. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19955245
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2787394/
- Perera MA, Cavallari LH, Limdi NA, Gamazon ER, Konkashbaev A, Daneshjou R, Pluzhnikov A, Crawford DC, Wang J, Liu N, Tatonetti N, Bourgeois S, Takahashi H, Bradford Y, Burkley BM, Desnick RJ, Halperin JL, Khalifa SI, Langaee TY, Lubitz SA, Nutescu EA, Oetjens M, Shahin MH, Patel SR, Sagreiya H, Tector M, Weck KE, Rieder MJ, Scott SA, Wu AH, Burmester JK, Wadelius M, Deloukas P, Wagner MJ, Mushiroda T, Kubo M, Roden DM, Cox NJ, Altman RB, Klein TE, Nakamura Y, Johnson JA. Genetic variants associated with warfarin dose in African-American individuals: a genome-wide association study. Lancet. 2013 Aug 31;382(9894):790-6. doi: 10.1016/S0140-6736(13)60681-9. Epub 2013 Jun 5.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23755828
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3759580/
- van der Zee SA, Halperin JL. Anticoagulant therapy: warfarin sensitivity genotyping closer to clinical practice. Nat Rev Cardiol. 2010 Oct;7(10):549-50. doi: 10.1038/nrcardio.2010.126.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20865027

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/CYP2C9

Reviewed: June 2015
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services